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BELL, BOYD & LLOYD LLP  
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EXAMINER
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CHOWDHURY, IQBAL HOSSAIN

ART UNIT	PAPER NUMBER
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1652

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	02/12/2007	PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

**Office Action Summary**

Application No.

10/070,038

Applicant(s)

BRUESSOW ET AL.

Examiner

Iqbal H. Chowdhury, Ph.D.

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 14 November 2006.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 1-5 and 7-33 is/are pending in the application.
- 4a) Of the above claim(s) 8, 11-17 and 33 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-5, 7, 9, 10 and 18-32 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some \* c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892)                     | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

## DETAILED ACTION

### *Application Status*

In view of the applicants response filed on 11/14/2006 showing that a bonafide response was filed in response to the Office action dated, 1/13/2006, the abandonment notice is withdrawn. Any inconvenience caused is deeply regretted.

Claims 1-5, 7-33 are currently pending in this application. Claims 8, 11-17, 33 remain withdrawn from consideration. Claims 1-5, 7, 9-10 and 18-32 are now under consideration in the instant Office action.

### *Election/Restriction*

Newly submitted claim 33 is directed to inventions that are independent or distinct from the invention originally elected for the following reasons: Newly added claim 33 depending from claim 5 is drawn to a S. thermophilus strain wherein the bacterial chromosome comprises addition of DNA at a site which disrupts expression of oxidoreductase gene. However, according to the original election without traverse applicants have elected claims 1-7, 9-10 and 18-27 as directed to a S. thermophilus strain comprising a modification in Øsf121 prophage such that it is resistant to attack by at least one bacteriophage and further comprises addition of DNA to the bacterial chromosome at a site which disrupts the expression of chorismate mutase. Therefore, newly added claim 33 is restricted to Group III.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution

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on the merits. Accordingly, claim 33 is withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03. Claims 1-5, 7, 9-10 and 18-32 will be examined to the extent of original election of Group I drawn to S. thermophilus which is resistant to at least one bacteriophage attack comprising a modification in Øsfi21 prophage wherein said modification is a deletion sufficient to disrupt prophage expression and wherein said bacterial chromosome comprises addition of DNA at a site in ORF-90 that disrupts only chorismate mutase chain A.

Applicants' arguments filed on November 14, 2006 have been fully considered but are not deemed to be persuasive to overcome some of the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn.

#### ***Withdrawn Claim Objections***

Previous objections to claims 1-10 and 18-27 are withdrawn in view of applicant's amendment of the claims.

#### ***New Claim Objections***

Claim 5, 28 and 32 are objected to as encompassing non-elected subject matter. These claims continue to recite non-elected subject matter such as "disruption of down-stream gene ORF394 and disruption of oxidoreductase gene" as alternative to elected subject matter of "disruption of chorismate mutase chain A". Examiner reminds applicants that the above non-elected subject matter were grouped under separate groups in the restriction mailed on 10/21/2005 and applicants have elected without traverse Group I, directed to S. thermophilus

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strain resistant to attack by another bacteriophage, which comprises a deletion in ØSfi21 prophage and an addition of DNA to the bacterial chromosome at a site that disrupts expression of chorismate mutase gene.

Claim 4 is objected to for the recitation “a sequence of bases ISS1”, as abbreviations should not be used without at least once fully setting forth what they are used for. Applicants’ need to expand “ISS1” abbreviation. Appropriate correction is required.

Claim 5 is objected to in the recitation “chosen”. Examiner suggests the use more appropriate term “selected”.

***Withdrawn Claim Rejections - 35 U.S.C. § 112(2<sup>nd</sup>)***

Previous rejection of claim 4 under 35 USC § 112, second paragraph, as being indefinite is withdrawn in view of applicant’s persuasive arguments.

***New-Claim Rejections - 35 U.S.C. § 112(2<sup>nd</sup>)***

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claim 4 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claim 4 is indefinite in the recitation of “a sequence of bases ISS1 or functional equivalent thereof” which is confusing. It is not clear what these sequences are and what is the “functional equivalent”. It would not be clear to those skilled in the art as to what function these sequences have unless the function is reiterated in the claim.

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Claims 7, 20, 24, 27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 7, 20, 24 and 27 recites a “bacteria according to claim 1 wherein the modification comprises a deletion of at least part of ORF1560”. It is not clear whether this ORF resides on the bacterial genome or the prophage. Since applicants have referred to other ORFs on the bacterial genome, it is highly imperative that applicants indicate where ORF1560 resides, without which it would be highly unclear to one of ordinary skill in the art.

Claims 9, 10, 21 and dependent claim 22-27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 9, 10 and 21 recite the phrase “substantially prevented”. The metes and bounds of the term “substantial” is not clear to the examiner. It is not clear as to how much prevention of phage propagation is considered as substantial by the applicants. Since the term is open ended and not correlated to any numerical value such as “percent” the metes and bounds of the phrase is highly unclear.

Claim 9, 10, 21 and dependent claim 22-27 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. Claims 9, 10 and 21 are indefinite in the recitation “sufficient DNA” as it is unclear as how much deletion of the DNA is encompassed by the phrase “sufficient DNA”.

***New-Claim Rejections - 35 USC § 112 (Deposit requirement)***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

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The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 2 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

The invention appears to employ novel microorganisms (Sfil and Sfilc16) comprising a modified gene due to insertion DNA material. Since the microorganisms are essential to the claimed invention, they must be obtainable by a repeatable method set forth in the specification or otherwise be readily available to the public. The recited microorganisms have not been shown to be publicly known and freely available. The enablement requirements of 35 § U.S.C. 112 may be satisfied by a deposit of the microorganisms. The specification does not disclose a repeatable process to obtain the microorganisms and it is not apparent if the microorganisms are readily available to the public. Accordingly, it is deemed that a deposit of these microorganisms should have been made in accordance with 37 CFR 1.801-1.809.

If the deposit is made under the terms of the Budapest Treaty, then an affidavit or declaration by applicants, or a statement by an attorney of record over his or her signature and registration number, stating that the specific strain has been deposited under the Budapest Treaty and that the strain will be available to the public under the conditions specified in 37 CFR 1.808, would satisfy the deposit requirement made herein.

If the deposit is not made under the Budapest treaty, then in order to certify that the deposit meets the criteria set forth in 37 CFR 1.801-1.809, applicants may provide assurance or compliance

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by an affidavit or declaration, or by a statement by an attorney of record over his or her signature and registration number, showing that:

1. during the pendency of this application, access to the invention will be afforded to the Commissioner upon request;
2. upon granting of the patent the strain will be available to the public under the conditions specified in 37 CFR 1.808;
3. the deposit will be maintained in a public repository for a period of 30 years or 5 years after the last request or for the effective life of the patent, whichever is longer; and
4. the deposit will be replaced if it should ever become unavailable.

***New-Claim Rejections - 35 USC § 112, First Paragraph (new matter)***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 9, 10 and 21 and dependent claims 22-27 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

Claims 9, 10 and 21 are directed to a composition comprising a S. thermophilus bacterial strain, which has been mutated in a Sfi21 prophage genome such that phage propagation within the bacterium is substantially prevented, wherein the mutation comprises deletion of sufficient



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DNA to disrupt expression of the prophage and at least one component chosen from the group consisting of a carrier, adjuvant and diluent.

There is no indication in the specification of the recitation "substantially prevented" as recited in the claims, within the scope of the invention as conceived by Applicants at the time the application was filed. Accordingly, Applicants are required to cancel the new matter in response to this Office Action.

***Maintained - Claim Rejections - 35 U.S.C. § 112(1<sup>st</sup>)***

Previous rejection of Claims 1-4, 6-7, 9-10 and 18-27 under 35 U.S.C. 112, first paragraph, enablement requirement, is maintained. This rejection has been described in length in previous Office Action. Applicant's arguments have been fully considered but are not deemed persuasive for the following reasons.

Claims 1, 3-5, 7, 9-10, 18-21, 23-24, 26-28, 30-32 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a modified S. thermophilus strain Sfi1 and Sfi16 comprising a ØSfi21 prophage, wherein said prophage is modified by deletion of sufficient DNA to disrupt expression of the prophage in the bacterium and wherein said S. thermophilus comprises a modification in the bacterial chromosome at ORF90 due to an insertional mutation comprising insertion of ISS1 leading to disruption in expression of the chorismate mutase chain A gene, and starter culture and milk products thereof comprising said S. thermophilus, does not reasonably provide enablement for modification of any or all S. thermophilus strains comprising ØSfi21 prophage with deletions, wherein said strain becomes resistant to attack by bacteriophage and wherein said strain further comprises a modification to

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its genomic DNA at ORF90 wherein said modification comprises insertion of any or all DNA sequence or functional equivalents of ISS1, including variants, and mutants of ISS1, and starter culture and milk products thereof comprising said bacterial strain. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Claims 1, 3-5, 7, 9-10, 18-21, 23-24, 26-28, 30-32 are so broad as to encompass any strain of S. thermophilus bacterium comprising a modified ØSfi21 prophage genome rendering said strain, resistant to attack by bacteriophage and starter culture and milk products thereof wherein said strain further comprises modification of its genomic DNA by addition of any or all DNA including functional equivalent of ISS1. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the S. thermophilus bacterium strains and any or all DNA comprising ISS1 including functional equivalents of ISS1 as encompassed in the above claims. While methods of preparing bacterial strains by mutating prophage genome and mutating bacterial chromosome by way of specific DNA integration using specific DNA sequences affecting the expression of specific bacterial genes are well known in the art, mutating bacterial chromosome or prophage genome in any S. thermophilus bacterial strain so as to produce a strain resistant to any phage infection is not routine wherein said bacterial genome is modified by insertion of any DNA affecting any gene on the bacterial genome. Knowledge of modification of S. thermophilus Sfi1 and Sfi16 strain chromosomes by addition of ISS1 in ORF90 disrupting expression of chorismate mutase or one modification in prophage ØSfi21 genome, rendering said bacterial strain resistant to attack by a specific bacteriophage in the said bacterium is unlikely to provide any guidance for producing mutants of any or all S.

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thermophilus bacterial strains resistant to infection by bacteriophage. However, in this case the disclosure is limited to mutants of two S. thermophilus strains comprising a modification in its prophage and its genome as explained above.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including modification of any S. thermophilus bacterial strain chromosome by adding any DNA or a functional equivalent of ISS1 gene anywhere on the genome affecting the expression of any bacterial genes as well as comprising a modified ØSfi21 prophage. The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, making any strain of S. thermophilus bacterium resistant to a phage attack by modifying prophage ØSfi21 and modifying the bacterial genome such that the mutant strain has the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Applicants argue that the modifications as recited in the claims are modifications that include addition of DNA at a specific site or deletion of DNA at a specific site and are not just "any" modifications of the Sfi21 prophage or the bacterial chromosome. Applicants also argue that the specification teaches disrupting expression of the prophage at ORF1560 of the Sfi21 prophage and the specification teaches disrupting expression of the chorismate mutase chain A gene at ORF90. Applicants further argue that the specification sets forth at page 14, lines 30-33 that this disruption of expression may prevent the interaction between phage

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structural proteins and bacterial structures required for DNA injection into the host and the methods for disrupting the expression of open reading frames, either in a plasmid, a (pro) phage or genome, are well known to the skilled person. In particular, the specification at page 4 discloses a number of well-known techniques, such as site-directed integration, transposition, assay for selection of phage-resistant mutants, etc., to disrupt host factors required at various steps of the bacteriophage life cycle such as DNA injection. Applicants furthermore argue that one must disrupt the expression of proteins involved in the infection process through the addition or deletion of DNA at a specific site that methods may comprise the generation of a plasmid allowing integration of DNA in a specific site(s) of the gene to be "knocked out" by single or double cross-over events and such a deletion may be carried out according to the deletions performed in ORF1560 as sufficiently described at page 9, lines 6-16 of the Specification. The Specification further sets forth at page 14, lines 9-11 that the mutant strain, Sfi1c16 $\Delta$ 1560, does not release detectable infectious particles upon challenge and plaque assays demonstrated additional suppression of phage infectivity of said bacterial strain (Table 2, of the present specification). Applicants concluded that the specification provides sufficient guidance to one of skill in the art to practice the claimed

Applicant's arguments have been fully considered but are not deemed to be persuasive to overcome the rejection of claims 1, 3-5, 7, 9-10, 18-21, 23-24, 26-28, 30-32. The examiner acknowledges the amendment to the claims but disagrees with the applicant's contention that the claimed invention is enabled for full scope claimed. Examiner has also rewritten the rejection in order to make the issue clear.

As mentioned in the previous Office Actions, instant claims are drawn to modification of any S. thermophilus bacterial strain by addition of any DNA or any DNA that comprises a sequence of bases of ISS1 or functional equivalent thereof as well as modification of prophage sfi21 genome by deletion part of ORF1650 or deletion of sufficient DNA to disrupt expression of prophage in the bacterium, wherein said S. thermophilus bacterial strain becomes resistant to attack by bacteriophage, and starter culture and milk products thereof. The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the large number of S. thermophilus strains, the number of DNA used to modify the bacterial genome and the number of genes in the bacterial genome that are affected due to addition of DNA, broadly encompassed by the claims. The scope of the claimed invention is very broad, and does not specify which part of DNA of prophage is deleted to disrupt the expression of prophage in said bacterium or which part of ORF1650 is deleted in the prophage genome as well as which specific DNA is added or which specific site on the bacterial genome resulting in the disruption of which specific gene.

As explained in the rejection, while methods of preparing a bacterial strain by mutating prophage genome and the bacterial chromosome are well known in the art, mutating bacterial chromosome or prophage genome in the bacterial strain so as to produce a strain resistant to any phage infection, as claimed is not routine. Knowledge of the modifications to S. thermophilus Sfi1 and Sfi16 bacterial chromosome (i.e. disrupting chorismate mutase chain A expression) or one modification in prophage genome, rendering said strains resistant to attack by a specific bacteriophage in the said bacterium does not provide any guidance for producing other mutants of any or all S. thermophilus. However, in this case the disclosure is limited to two mutants of S.

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thermophilus comprising a modified ØSfi21 prophage and specific addition of ISS1 DNA to the bacterial genome at ORF90 such that the expression of chorismate mutase gene is disrupted.

In response to applicant's arguments that "the modifications as recited in the claims are modifications that include addition of DNA at a specific site or deletion of DNA at a specific site", Examiner respectfully disagrees. This is because the amendments do not indicate which specific portions of prophage is deleted or which specific DNA is added affecting which specific bacterial gene. Instant amended claims do not provide sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, making strains of S. thermophilus bacterium resistant to phage attack by modifying prophage ØSfi21 as well as modifying the bacterial genome such that the mutant strain has the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). Therefore, the rejection is maintained.

***Withdrawn-Claim Rejections - 35 USC § 102***

Previous rejection of Claims 1, 3-4, 9-10, 19, 21, 23 and 26 under 35 U.S.C. 102(b) as being anticipated by Sturino et al. ("Construction of bacteriophage resistant strains of *Streptococcus thermophilus* by pGh9::ISS1 insertional mutagenesis", *Journal of Dairy Science*, vol. 81, no. Suppl. 1, 1998, p. 7, Joint Meeting of the American Society for Animal Science; Denver, Colorado, USA; July 28-31, 1998, see IDS) is withdrawn in view of Applicants

amendment of claims and persuasive arguments.

***Maintained-Claim Rejections - 35 USC § 102***

Previous rejection of Claims 1-2 7, 9-10, 18, 20, 22, 24, 28-31 under 35 U.S.C. 102(b) as being anticipated by Foley et al. ("A short noncoding viral DNA element showing characteristics of a replication origin confers bacteriophage resistance to *Streptococcus thermophilus*", Virology. 1998 Oct 25; 250(2): 377-87, see IDS) is maintained. This rejection has been described in length in previous Office Action. Applicant's arguments have been fully considered but are not deemed persuasive for the following reasons.

Instant claims are directed to a *S. thermophilus* Sfi1 or Sfi16 resistant to attack by at least one bacteriophage and which comprises a modification of a Øsfi21 prophage, wherein the Øsfi21 prophage is modified by deletion of sufficient DNA to disrupt expression of the prophage in the bacterium.

Applicants argue that Foley et al. do not disclose preventing replication and propagation of phage within the cell by deletion of DNA in the Øsfi21 prophage genome sufficient to prevent expression of the prophage and Foley et al. describes a non-coding DNA fragment present in the genome of the Øsfi21 phage thought to act as an origin for DNA replication of the phage. Applicants also argue that the non-coding DNA fragment is not deleted from the DNA replication module of Øsfi21 as suggested in the Office Action, page 9, but is cloned into a shuttle vector to be added to the Sfi1 strain of *S. thermophilus* to transform the bacterium. Therefore, Foley does not teach or suggest an *S. thermophilus* bacterial strain which has been mutated by deletion of sufficient DNA in a Øsfi21 prophage genome to disrupt expression

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of the prophage such that phage propagation within the bacterium is substantially prevented as in the claimed invention. At the end, Applicants requested to withdraw the rejection.

Applicant's arguments have been considered but are not deemed persuasive to overcome the rejection. First of all, contrary to applicants arguments claims are not limited to a strain of S. thermophilus in which replication or propagation of the phage ØSfi21 is prepared. Indeed, claims are simply limited to a S. thermophilus that has been rendered resistant to at least one bacteriophage wherein said bacterial strain comprises a modified Øsfi21 prophage by deletion of "sufficient DNA" to disrupt expression of said prophage in the bacterium. Foley et al. teach such a strain comprising a modified prophage wherein introduction of said modified prophage into S. thermophilus renders it resistant to attack by bacteriophage. Claims are limited to the bacterial strain comprising any type of modified prophage. Furthermore, contrary to applicants argument, the reference does teach a S. thermophilus in which the replication and propagation of the full bacteriophage is prevented. Foley's description of non-coding DNA fragment present in the Øsfi21 phage is thought to act as an origin for DNA replication of the phage. However, the presence of such a fragment in S. thermophilus cells does not lead to propagation of the phage in the bacterial cell. Rather, the reference clearly demonstrates that its presence in the bacterial cell makes it resistant to attack by at least one bacteriophage.

As discussed previously, Foley et al teach S. thermophilus strains having a modified phage phiSfi21, wherein said modification is the deletion of sufficient DNA, which results in a S. thermophilus strain Sfi1 resistant from infection by 17 of 25 phages. Therefore, Foley et al. clearly anticipate claims 1-2 7, 9-10, 18, 20, 22, 24, 28-31 as written and the rejection is maintained.



***Withdrawn-Claim Rejections - 35 USC § 103***

Previous rejection of Claims 22, 24-25, and 27 under 35 U.S.C. 103(a) as being unpatentable over Sturino et al. ("Construction of bacteriophage resistant strains of *Streptococcus thermophilus* by pGh9::ISS1 insertional mutagenesis", Journal of Dairy Science, vol. 81, no. Suppl. 1, 1998, p. 7, Joint Meeting of the American Society for Animal Science; Denver, Colorado, USA; July 28-31, 1998, see IDS) in view of Foley et al. ("A short noncoding viral DNA element showing characteristics of a replication origin confers bacteriophage resistance to *Streptococcus thermophilus*", Virology. 1998 Oct 25; 250(2): 377-87, see IDS) is withdrawn without acquiescing to applicants arguments.

***New-Claim Rejections - 35 USC § 103***

Claims 3-4, 19, 21, 23, 25-27 are rejected under 35 U.S.C. 103(a) as being unpatentable over Foley et al. ("A short noncoding viral DNA element showing characteristics of a replication origin confers bacteriophage resistance to *Streptococcus thermophilus*", Virology. 1998 Oct 25; 250(2): 377-87, see IDS) as applied to claims 1-2 7, 9-10, 18, 20, 22, 24, 28-31 and further in view of Sturino et al. ("Construction of bacteriophage resistant strains of *Streptococcus thermophilus* by pGh9::ISS1 insertional mutagenesis", Journal of Dairy Science, vol. 81, no. Suppl. 1, 1998, p. 7, Joint Meeting of the American Society for Animal Science; Denver, Colorado, USA; July 28-31, 1998, see IDS) and the common knowledge in the art regarding the use of *S. thermophilus* for making milk products.

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Instant claims are directed to a *Streptococcus thermophilus* resistant to attack by at least one bacteriophage and which comprises a modification of an Øsfi21 prophage, wherein the Øsfi21 prophage is modified by deletion of sufficient DNA to disrupt expression of the prophage in the bacterium, and wherein the bacterial chromosome is also modified by the addition of DNA comprising ISS1 or functional equivalent, and milk products comprising said S. thermophilus.

Foley et al teach a S. thermophilus strain comprising a modified Øsfi21 prophage wherein the modification i.e. deletion of a DNA fragment from the DNA as explained under 102 rejection above, which results in a Streptococcus thermophilus strain Sf11 resistant from infection by 17 of 25 phages including phiSfi21. Foley et al. do not teach the further modification of such strains by addition of DNA comprising ISS1 into the bacterial chromosome or use of said bacteria or milk products comprising said modified bacteria.

However, Sturino et al teach the construction of bacteriophage resistant strains of *S. thermophilus* by addition of DNA comprising ISS1 by insertional mutagenesis. Sturino et al further teach the use of such resistant strain in the fermentation process in the milk industry as a starter culture.

By combining the teachings of Foley et al. and Sturino et al. it would have been obvious to one of ordinary skill in the art to modify a *S. thermophilus* bacterium containing deleted phage genome as taught by Foley et al., by further adding DNA comprising ISS1 DNA to the bacterial genome as taught by Sturino et al. to make *S. thermophilus* strains more resistant to phage attacks.

One of ordinary skill in the art would have been motivated to do so in order to arrive at S. thermophilus strains that are fully resistant to phage attacks during their use in fermenting milk,

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thereby prevent loss of starter activity.

One of ordinary skill in the art would have a reasonable expectation of success because both the above references individually teach and successfully demonstrate the making of phage resistant S. thermophilus strains using two different techniques.

Therefore, the above references render the claims 3-4, 19, 21, 23, 25-27-*prima facie* obvious to one of ordinary skill in the art.

### ***Conclusion***

Claims 1-5, 7-33 are pending.

Claims 8, 11-17 and 33 remain withdrawn.

Claims 1-5, 7, 9-10, 18-32 stand rejected.

No claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a).

Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 C.F.R. 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Iqbal Chowdhury, Ph.D. whose telephone number is 571-272-8137. The examiner can normally be reached on 9:00-5:00.

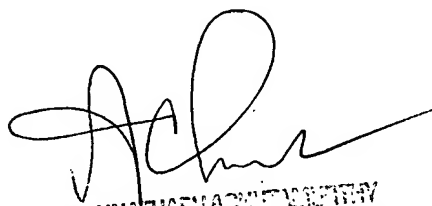
If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ponnathapu Achutamurthy can be reached on 703-272-0928. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

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